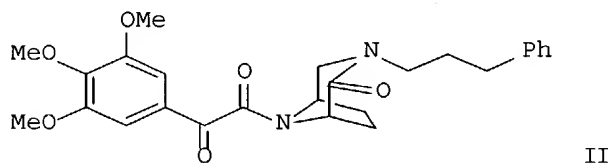
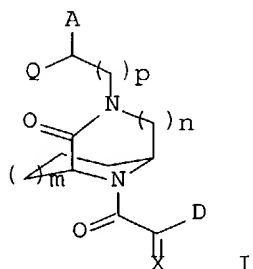


L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2001:435076 CAPLUS Full-text  
 DN 135:46205  
 TI Preparation of neurotrophic bicyclic diamides with peptidylprolyl  
 isomerase (PPIase or rotamase) inhibitory activity  
 IN Dubowchik, Gene Michael; Provencal, David Paul  
 PA Bristol-Myers Squibb Company, USA  
 SO PCT Int. Appl., 91 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001042245	A1	20010614	WO 2000-US32395	20001128
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1999-169600P	P	19991208		
OS	MARPAT 135:46205				
GI					



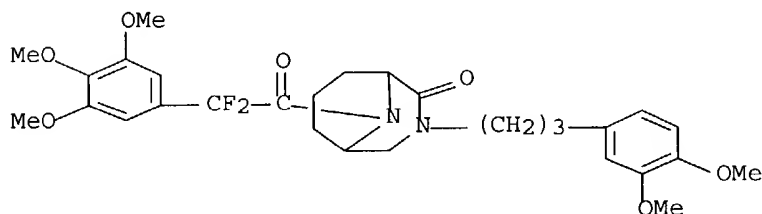
AB The invention relates to the design, synthesis, and the peptidylprolyl  
 isomerase (PPIase or rotamase) inhibitory activity of novel bicyclic  
 diamide compds. that are neuroprotective and/or neurotrophic agents  
 (i.e. compds. capable of stimulating growth or proliferation of nervous  
 tissue), and that bind to immunophilins such as FKBP12 and inhibit their  
 rotamase activity. This invention also relates to pharmaceutical  
 compns. comprising these compds. The compds. are encompassed by  
 structure I [X = O, F<sub>2</sub>; n = 1, 2; m = 0, 1, 2; p = 0, 1; D = alk(en)yl,  
 cycloalk(en), alk(en)yl, 2- or 3-indolyl, Ar, Ar-alk(en)yl; Ar =  
 selected (un)substituted carbo- or heterocyclic aromatic groups; Q, A =  
 H, Ar, alk(en/yn)yl, cycloalk(en)ylalk(en/yn)yl, their N/O/S-heteroat.  
 analogs, etc.; and their pharmaceutically acceptable salts]. Over 40  
 examples were prepared and tested. For instance, (1S,5R)-8-benzyl-3,8-  
 diaza-3-(3-phenylpropyl)bicyclo[3.2.1]octan-2-one (preparation given)  
 underwent hydrogenolytic debenzoylation and amidation with 3,4,5-  
 trimethoxyphenyl-2-oxoacetyl chloride to give title compound II. In a  
 fluorescence polarization assay of FKBP12 binding, II gave 34%  
 inhibition at 1  $\mu$ M, and its 3-(3-pyridyloxy)propyl analog gave 98%  
 inhibition.

IT 344462-06-2P 344462-07-3P 344462-08-4P  
344462-09-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (stereoselective preparation and biol. activity of bicyclic diamides as neuroprotective agents and peptidylprolyl isomerase (PPIase or rotamase) inhibitors)

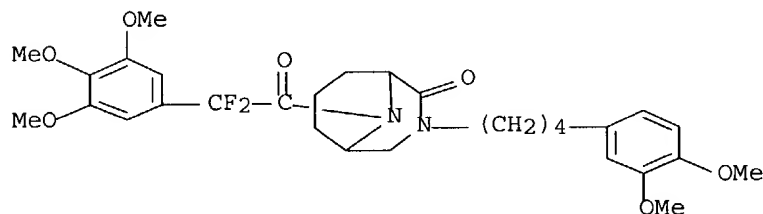
RN 344462-06-2 CAPLUS

CN 3,9-Diazabicyclo[3.3.1]nonan-2-one, 9-[difluoro(3,4,5-trimethoxyphenyl)acetyl]-3-[3-(3,4-dimethoxyphenyl)propyl]- (9CI) (CA INDEX NAME)



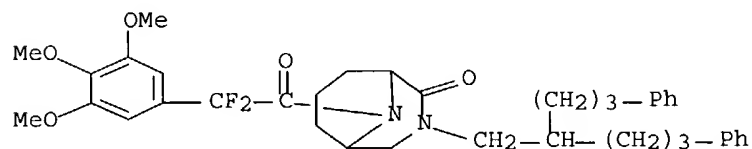
RN 344462-07-3 CAPLUS

CN 3,9-Diazabicyclo[3.3.1]nonan-2-one, 9-[difluoro(3,4,5-trimethoxyphenyl)acetyl]-3-[4-(3,4-dimethoxyphenyl)butyl]- (9CI) (CA INDEX NAME)



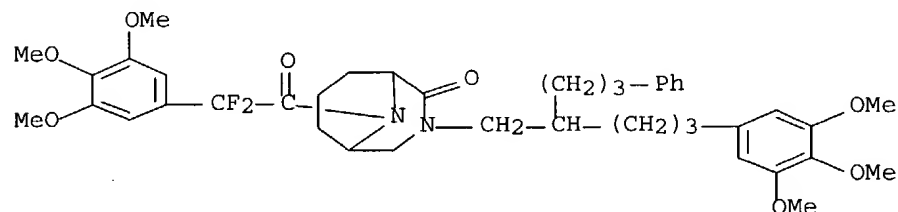
RN 344462-08-4 CAPLUS

CN 3,9-Diazabicyclo[3.3.1]nonan-2-one, 9-[difluoro(3,4,5-trimethoxyphenyl)acetyl]-3-[5-phenyl-2-(3-phenylpropyl)pentyl]- (9CI) (CA INDEX NAME)



RN 344462-09-5 CAPLUS

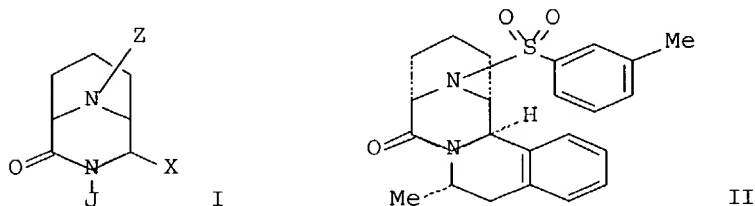
CN 3,9-Diazabicyclo[3.3.1]nonan-2-one, 9-[difluoro(3,4,5-trimethoxyphenyl)acetyl]-3-[2-(3-phenylpropyl)-5-(3,4,5-trimethoxyphenyl)pentyl]- (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

L7 ANSWER 1 OF 1 MARPAT COPYRIGHT 2004 ACS on STN  
 AN 137:370075 MARPAT Full-text  
 TI Preparation of diazabicyclo[3.3.1]nonane derivatives as FKBP-ligands  
 IN Guo, Chuangxing; Augelli-Szafran, Corinne E.; Barta, Nancy Sue; Bender, Steven Lee; Bigge, Christopher Franklin; Caprathe, Bradley William; Chatterjee, Arindam; Deal, Judith; Dong, Liming; Fay, Lorraine Kathleen; Hou, Xinjun; Hudack, Raymond Andrew, Jr.  
 PA Agouron Pharmaceuticals, Inc., USA; Warner-Lambert Company  
 SO PCT Int. Appl., 177 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002089806	A1	20021114	WO 2002-US14966	20020510
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP	1423119	A1	20040602	EP 2002-731761	20020510
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRAI	US 2001-289828P		20010510		
	WO 2002-US14966		20020510		
GI					

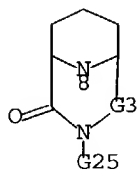


AB Title compds. I [Z = sulfonyl, acyl, etc.; J = H, alk(en)yl, cycloalkyl, aryl, heteroaryl; X = H, CN, alkoxy, dimethoxymethyl, oxygen (when the C-X bond is a double bond); X, J taken together with the N to form a (un)substituted heteroaryl, heterocycloalkyl] were prepared Over 130 example compds. were prepared and tested. For instance, 2,6-pyridinedicarboxylic acid was reduced to the corresponding cis-piperidine dicarboxylic acid (H<sub>2</sub>O, NaOH, H<sub>2</sub>-Rh/Al, 55 psi, 48 h) and converted to the N-Cbz derivative This intermediate was converted to the bicyclic anhydride (Ac<sub>2</sub>O, 70°) and subsequently reacted with L-amphetamine to provide the corresponding imide (Ac<sub>2</sub>O, 110°). Reduction of the imide (THF/MeOH, NaBH<sub>4</sub>, -5°, 55 min), cyclization (CH<sub>2</sub>Cl<sub>2</sub>, TFA), removal of the Cbz group (EtOH/EtOAc, H<sub>2</sub>-Pd/C) and sulfonylation with m-toluenesulfonyl chloride provided II. Compds. of the invention inhibit FKBP-12 rotamase (peptidyl-prolyl isomerase) activity; II had K<sub>i</sub> = 0.32 μM. I are useful for the treatment of peripheral neuropathies.

MSTR 1

G7—G1

G1 = 8



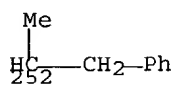
G3 = 75

H<sub>5</sub>—G4

G7 = 198

<sup>198</sup>G(O)-CF<sub>2</sub>-G8

G25 = 252



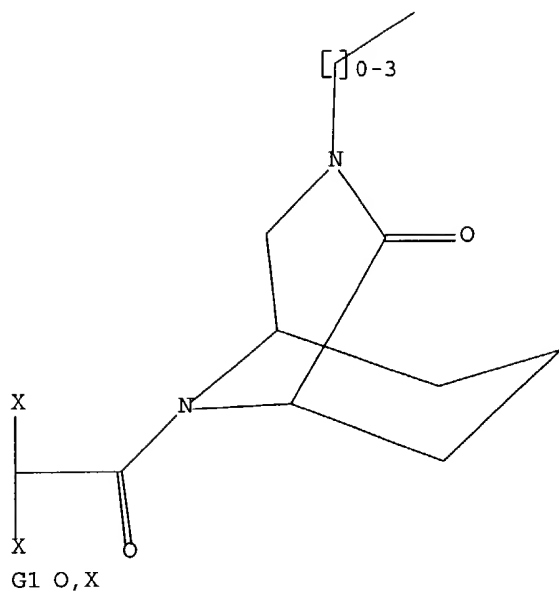
MPL: claim 1

NTE: also incorporates claim 15

NTE: or pharmaceutically acceptable salts, solvates, prodrugs, or pharmacologically active metabolites

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l1; d his; log y  
 L1 HAS NO ANSWERS  
 L1 STR



Structure attributes must be viewed using STN Express query preparation.

(FILE 'HOME' ENTERED AT 18:39:55 ON 02 JUN 2004)

FILE 'REGISTRY' ENTERED AT 18:40:02 ON 02 JUN 2004

L1 STRUCTURE UPLOADED  
 L2 0 S L1  
 L3 4 S L1 FUL

FILE 'CAPLUS' ENTERED AT 18:40:28 ON 02 JUN 2004

L4 1 S L3

FILE 'BEILSTEIN' ENTERED AT 18:40:57 ON 02 JUN 2004

L5 0 S L1 FUL

FILE 'MARPAT' ENTERED AT 18:41:11 ON 02 JUN 2004

L6 2 S L1 FUL  
 L7 1 S L6 NOT L4

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	114.29	275.17
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-0.66	-1.35

STN INTERNATIONAL LOGOFF AT 18:42:34 ON 02 JUN 2004